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CORRESPONDENCE

A need to revise ciprofloxacin breakpoints for Salmonella in human beings

The indiscriminate use of ciprofloxacin for the treatment of typhoid fever has been accompanied by a frightening increase in the number of resistant cases. Isolates of *Salmonella* Typhi with reduced susceptibility to ciprofloxacin (as indicated by an increase in minimum inhibitory concentration (MIC)), but still within the current Clinical and Laboratory Standards Institute (CLSI) range for susceptibility (≤1 μg/ml), have appeared in the Indian subcontinent and other regions.[1,2] Reduced susceptibility to ciprofloxacin is mediated by a single mutation in the *gyrA* gene.[3]

A study was conducted at our center on 127 Salmonella isolates obtained from blood cultures of patients during the period January 2006 to May 2007 to determine the MIC of ciprofloxacin by agar dilution method.[4] The concentrations used were doubling dilutions of ciprofloxacin from 0.0625 μg/ml to 32.0 μg/ml. The antibiotic susceptibilities of ciprofloxacin and nalidixic acid were also determined by Kirby—Bauer disc diffusion technique.

An increase in the MIC for ciprofloxacin (0.125—2.0 μg/ml) was noted despite 100% susceptibility by disc diffusion method (Table 1). Resistance to nalidixic acid was high (95.4% for *Salmonella* Typhi and 92.5% for *Salmonella* Paratyphi A). Nalidixic acid resistance is a marker for predicting low-level resistance to ciprofloxacin and also an indicator of treatment failure.

During 1989—90, there were reports of fever subsiding after a mean of 3 days of ciprofloxacin therapy.[5] From 1993, reports of fever subsiding only after 5—6 days of treatment appeared.[6] In one community-based study, 21.9% of cases took longer than 8 days to become afebrile and 9% did not respond even after 15 days of treatment, despite in vitro susceptibility.[7] In a study conducted on patients from seven US states, patients with *Salmonella* Typhi infection with ciprofloxacin MICs of 0.12—1 μg/ml had a mean fever clearance time of 90 hours, as compared with patients infected with isolates with ciprofloxacin MICs <0.12 μg/ml where it was 64 hours.[8] In another study, *Salmonella* Typhi was recovered from blood after 6 days of ciprofloxacin therapy in 17.4% of the patients who experienced treatment failure.[9]

The use of high ciprofloxacin breakpoints not only misguides clinicians, but also affects the surveillance of resistance to this important drug and thus hinders the formulation of policies for rational drug usage. Hence, to minimize the probability of clinical failure or delayed response, and to assess the true magnitude of antibiotic resistance, a lower breakpoint for ciprofloxacin is recommended. Booker et al. suggested susceptible breakpoints of 0.12 μg/ml in an in vitro infection model.[10] Moreover, changing susceptibility breakpoints will negate the need for the use of the nalidixic acid screening test.

Conflict of interest: No conflict of interest to declare.

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Table 1 Minimum inhibitory concentration (MIC) values of ciprofloxacin for *Salmonella* Typhi *and Salmonella* Paratyphi isolates

Organism	No. of strains showing MIC (μg/ml) values of:							
	0.0625	0.125	0.25	0.5	1	2	4	8
Salmonella Paratyphi (40)	—	9	26	3	2	—	—	—
Salmonella Typhi (87)	—	6	11	62	5	3	—	—

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